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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,505	07/31/2001	Walter Ausserer	100/11630	2767

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EXAMINER	
BARTON, JEFFREY THOMAS	
ART UNIT	**PAPER NUMBER**
1753	

DATE MAILED: 10/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/919,505	AUSSERER ET AL.
	Examiner	Art Unit
	Jeffrey T. Barton	1753

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20020201, 20011203*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

1. The disclosure is objected to because application 09/859,962, to which priority is claimed, was converted to provisional application 60/327,566. In addition, the filing date of 60/327,566 is in our records as May 17, 2001, not May 15, 2001. Please amend the Related Applications section accordingly.

Appropriate correction is required.

Claim Objections

2. Claims 8, 9, 19-34, 40, 42, and 50 are objected to because of the following informalities:

a. Claim 8 is a duplicate of claim 2.

b. Claim 9 refers to "negative pressure", which technically does not exist. (i.e. zero pressure is absolute vacuum) "Reduced pressure" or "partial vacuum" might be more appropriate. The claim is treated herein as requiring reduced pressure.

c. In claims 19-34, dependency appears to be improperly stated. In order to have proper antecedent basis for "replacing step" and "second sample material" in claims 19-25 and 28, the examiner believes dependency on claim 18 was intended. In addition, given the grouping, claims 26 and 27 are also treated as dependent upon claim 18.

d. In claim 40, dependency appears to be improperly stated. To avoid improper antecedent basis for "mixture", the claim is treated herein as being dependent upon claim 35.

e. In claim 42, at line 8, after the phrase "wherein the", please replace the word "ample" with the word --sample--.

f. In claim 50, at line 2, please replace the word "I" with the word --in-- after the word "replaced".

Appropriate correction is required.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 18, 26, 27, 41, and 43-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Adourian et al.

Regarding claim 18, Adourian et al disclose a method comprising: providing a separation conduit with a separation matrix disposed therein (Column 3, lines 24-28);

transporting a first sample through the separation conduit for separation into a plurality of fractions (Column 13, lines 45-51); replacing the separation matrix; and transporting a second sample through the separation conduit. (Column 24, lines 2-20)

Regarding claim 26, Adourian et al disclose this method being carried out in a conduit with microscale dimensions. (Column 16, lines 52-58)

Regarding claim 27, Adourian et al disclose the conduit being disposed in a microfluidic device. (Abstract)

Regarding claim 41, Adourian et al disclose a separation system comprising a separation conduit, having a first flow resistance, filled with a flowable separation matrix (Column 3, lines 24-28); a sample loading conduit connected to the separation conduit, having a second flow resistance (Figures 8A-8C); a sample loading system for transporting material into the sample loading conduit (Column 13, lines 39-45); wherein the first flow resistance is higher than the second flow resistance by an amount sufficient to prevent substantial matrix displacement in the separation conduit. (Figures 8A-8C; Column 14, lines 1-6; Column 20, lines 39-54; all channels appear to have same cross-sectional area; length will result in higher flow resistance in separation conduit)

Regarding claim 43, Adourian et al disclose a microfluidic device comprising a body structure (Figure 10), and connected sample loading and separation channels, wherein the dimensions of the loading channel provide lower flow resistance than the separation channel. (See above)

Regarding claim 44, dimensions listed (30-300+ mm separation channel, 10 mm loading channel; Column 20, lines 39-54) would lead to the separation channel having more than twice the flow resistance of the loading channel.

Regarding claim 45, Adourian et al disclose an external pipettor element included on the sample loading channel. (Figure 3)

Regarding claims 46 and 47, Adourian et al disclose the separation and injection channels meeting at intermediate points in both channels. (Figures 8A-8C)

5. Claims 35, 36, and 40 rejected under 35 U.S.C. 102(b) as being anticipated by Ramsey.

Regarding claim 35, Ramsey discloses a method comprising: providing a system (Figure 30) that comprises a separation conduit (34G) with a separation matrix (Column 30, lines 23-31), a sample loading conduit in communication with the separation conduit (Reaction chamber - 18G), and sources of sample material and reagent in communication with the loading conduit (12G, 14G); transporting the sample material and reagent to the loading conduit (Column 28, line 47 - Column 29, line12), where they react; injecting a portion of the mixture into the separation conduit (Column 29, lines 6-7); and separating the mixture. (Column 28, lines 36-41)

Regarding claim 36, Ramsey discloses the first reagent comprising a labeling reagent. (Column 28, lines 36-41)

Regarding claim 40, Ramsey discloses injection by electrokinetics. (Column 7, lines 18-33)

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-10, 12-14, 17, 28-34, 48, 49, and 52-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adourian et al in view of Taylor et al.

Relevant to claims 1 and 48, Adourian et al disclose a method of separating a sample material into a plurality of fractions, comprising: providing a system comprising a separation conduit with gel (Column 3, lines 24-28) and a sample loading conduit in fluid communication with the separation conduit (Figures 8A-8C); flowing a sample into the sample loading conduit without substantially displacing the separation matrix from the separation conduit (Column 13, lines 39-47; Column 24, lines 2-20; repeated use for 20 runs - there cannot be substantial movement); injecting a portion of the sample into the separation conduit (Column 13, lines 47-49); electrophoretically separating the material into a plurality of fractions (Column 13, lines 49-51); and replacing the separation matrix and repeating the analysis with a new sample. (Column 24, lines 2-20)

Relevant to claims 28-34, Adourian et al disclose a method as described above in addressing claim 18.

Relevant to claims 2 and 8, Adourian et al disclose a sample loading conduit with a loading end in contact with sample material and a waste end. (Column 13, lines 39-45; Figures 8A-8C)

Relevant to claims 3-5, Adourian et al disclose no substantial displacement of the matrix. (Column 24, lines 2-20; repeated use for 20 runs - there cannot be substantial movement)

Relevant to claims 6 and 7, Adourian et al disclose a separation conduit that is longer than the injection conduit, that would result in a higher flow resistance. (Column 20, lines 39-54)

Relevant to claims 10 and 32, Adourian et al disclose the loading and separation conduits meeting at a junction, and the injection step comprising moving sample along the injection conduit, through this junction, and into the separation channel (Figures 8A-8C)

Relevant to claims 12, 13, 33, and 34, Adourian et al disclose the injection and separation being by electrophoresis. (Column 13, lines 39-51)

Relevant to claims 14 and 31, Adourian et al disclose the separation conduit being in fluid communication with a source of separation matrix, and the application of a pressure difference (via syringe) to transport this matrix into the conduit after a separation. (Column 21, lines 15-27; Column 24, lines 2-20)

Relevant to claim 49, Adourian et al disclose the entire separation matrix being replaced. (Column 24, lines 2-20)

Relevant to claim 52, Adourian et al disclose repeating analyses for numerous samples. (Column 24, lines 2-20)

Adourian et al do not explicitly disclose bulk flow of the samples through the sample loading conduit (Claim 1), application of pressure differences to cause fluid flow (Claims 2, 8, 28, 30), application of reduced pressure to the waste end of the injection channel to cause sample flow (Claims 9, 29), or no separation matrix being disposed in the sample loading conduit. (Claim 17)

Relevant to claims 1, 2, 8, and 9 Taylor et al disclose bulk flow of process fluids caused by application of pressure differences, including application of vacuum, to device ports and across channels in their device. (Column 2, lines 23-45; Column 6, lines 60-65) Relevant to claim 17, Taylor et al disclose a device with separation medium in the separation channel, but none disposed in the sample introduction channel. (Column 3, lines 1-15)

It would have been obvious to one having ordinary skill in the art to modify the method of Adourian et al by providing sample loading using the application of pressure gradients (e.g. by application of vacuum to the waste port), as taught by Taylor et al, because it is a known, conventional means of causing fluid flow in capillary devices, and would avoid sample biasing.

The application of pressure across the sample loading conduit would force separation medium from the injection channel, also resulting in reduced premature sample separation prior to injection, and meeting the limitations of claim 17. Given disclosed dimensions of the device (10 mm injection channel/300 mm separation channel), selection of appropriate pressure gradients (within the level of ordinary skill in the art) would lead to no substantial displacement of separation medium within the separation channel, provided the injection port is not closed.

Regarding claim 30, it would be obvious to use the same pressure difference, because it would allow the use of a single pressure or vacuum source.

Regarding claims 53 and 54, it would be obvious to perform the replacing and sample loading steps as a single step of vacuum application at the waste reservoir (i.e.

apply vacuum while pushing used matrix out with new matrix from a syringe/reservoir, then applying sample to the loading port), because it would reduce the number of process steps.

10. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adourian et al and Taylor et al as applied to claim 10 above, and further in view of Dubrow et al. (U.S. 5,976,336)

Adourian et al and Taylor et al disclose a combined method as described above in addressing claim 10.

Neither Adourian et al nor Taylor et al explicitly disclose the first fluid junction comprising a channel segment connecting the sample loading conduit with the separation conduit.

Dubrow et al disclose similar microfluidic devices and methods, including a method of preloading a subsequent sample in a device configured such that the sample loading conduit is connected to the separation channel by a distinct channel segment. (Figure 1G)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combined method of Adourian et al and Taylor et al by performing it in a device configured to have loading channels connected to a separation channel by distinct channel segments, as taught by Dubrow et al, because it would simplify sequential injections in devices (such as that of Adourian) designed for multiple sequential analyses. (e.g. less need for port rinsing)

11. Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adourian et al and Taylor et al as applied to claim 1 above, and further in view of Ramsey.

Adourian et al and Taylor et al disclose a combined method as described above in addressing claim 1. In addition, Adourian et al disclose the analysis of previously labeled samples. (Column 18, lines 22-27)

Neither Adourian nor Taylor explicitly disclose performing their methods in a device comprising a sample loading conduit in fluid communication with a reagent of any kind, wherein the sample and reagent are mixed during injection.

Ramsey discloses similar microfluidic devices and methods including a separation method (and corresponding device geometry) in which a sample and labeling reagent are mixed in the loading channel prior to injection on the separation column. (Column 28, lines 17-46)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combined method of Adourian et al and Taylor et al by performing it in a device that would allow the necessary labeling reactions to be performed immediately prior to sample injection, and running these reactions in the device prior to injection, as taught by Ramsey, because it would allow more of the required analytical steps to be automated within a single device.

12. Claims 19-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adourian et al in view of Nakajima et al.

Adourian et al disclose a method as described above in addressing claim 18.

Adourian et al do not explicitly disclose replacing only portions of the separation matrix.

Nakajima et al disclose a method of improving the performance of previously used chromatographic columns of any size (Column 2, lines 61-62) by replacing a portion of the separation matrix with fresh material. (Column 4, line 66 - Column 5, line 9) Examples are given from 4-65% replacement. (Table 1)

Relevant to claims 19-24, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Adourian et al by replacing only a portion of the separation matrix after a number of runs, as taught by Nakajima et al, because it would conserve separation medium. Additionally, if performed in an automated system after each run, it would help maintain consistent run-to-run matrix performance.

Regarding claim 25, it would also be obvious to replace any fraction of the gel that would provide beneficial results, which could be determined by one of ordinary skill in the art.

13. Claims 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramsey in view of Taylor et al.

Ramsey discloses a device as described above in addressing claim 35.

Relevant to claim 38, Ramsey discloses determination of exact ratios of combination of the sample and reagent. (Column 28, lines 58-62)

Ramsey does not explicitly disclose flow of the samples through the sample loading conduit by application of pressure differences to cause fluid flow (Claims 37 and 38), or application of reduced pressure to the waste end of the injection channel to cause sample flow. (Claim 39)

Taylor et al disclose bulk flow of process fluids caused by application of pressure differences, including application of vacuum, to device ports and across channels in their device. (Column 2, lines 23-45; Column 6, lines 60-65)

It would have been obvious to one having ordinary skill in the art to modify the method of Adourian et al by providing sample loading using the application of pressure gradients (e.g. by application of vacuum to the waste port), as taught by Taylor et al, because it is a known, conventional means of causing fluid flow in capillary devices, and would avoid sample biasing.

In addition, relevant to claim 38, it would be obvious to vary the dimensions of the channels to determine the ratio at which the reagent and sample are mixed, based on the requirements of the sample and reagent needed for the analysis, especially given the exactness with which Ramsey determined this ratio.

14. Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ramsey in view of Adourian et al and Taylor et al.

Ramsey discloses a system (Figure 30) comprising a separation conduit (34G) with a separation matrix (Column 30, lines 23-31), a sample loading conduit in communication with the separation conduit (Reaction chamber - 18G), and sources of sample material and reagent in communication with the loading conduit. (12G, 14G) Ramsey also discloses determination of exact ratios of combination of the sample and reagent. (Column 28, lines 58-62)

Ramsey does not explicitly disclose a system comprising a flowable matrix, or a pressure or vacuum source coupled to the sample loading conduit (which would provide bulk flow).

Adourian et al discloses a system in which the separation channels are filled with a flowable matrix in order to allowed continued use of the device indefinitely. (Column 24, lines 2-20)

Taylor et al disclose a microfluidic system coupled to a vacuum or pressure source to cause fluid motion in the channels. (Column 2, lines 23-45; Column 6, lines 60-65) They also disclose variation of the channel cross-section to vary the flow characteristics. (Column 5, lines 11-15)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the system of Ramsey by replacing his separation matrix with the flowable matrix of Adourian et al, because it would allow easy matrix replacement and continued use of a chip, thereby reducing costs.

Furthermore, it would have been obvious to modify the system of Ramsey by providing a pressure or vacuum source coupled to one or more of the ports of the

device to provide bulk flow, as taught by Taylor et al, because it would eliminate concerns of electrophoretic bias in injected samples and it is a known, conventional means of fluid transport in capillary systems.

In addition it would be obvious to choose dimensions of the sample and reagent conduits, as suggested by Taylor et al, to adjust the ratio of their combination, which was precisely determined by Ramsey, according to the requirements of the sample and reagent used in a particular analysis.

15. Claims 50 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adourian et al and Taylor et al as applied to claim 48 above, and further in view of Nakajima.

Adourian et al and Taylor et al disclose a combined method as described above in addressing claim 48.

Neither Adourian et al nor Taylor et al explicitly disclose replacing only portions of the separation matrix.

Nakajima et al disclose a method of improving the performance of previously used chromatographic columns of any size (Column 2, lines 61-62) by replacing a portion of the separation matrix with fresh material. (Column 4, line 66 - Column 5, line 9) Examples are given from 4-65% replacement. (Table 1)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Adourian et al by replacing only a portion of the separation matrix after a number of runs, as taught by Nakajima et al, because it

would conserve separation medium. Additionally, if performed in an automated system after each run, it would help maintain consistent run-to-run matrix performance.

Conclusion

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB
October 26, 2004

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